Debate: This house believes that SBRT should become the standard of care for T1 and small T2 NSCLC tumours

SP-0302
For the motion
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The current standard of care for T1 and small T2 early-stage non-small cell lung cancer (NSCLC) is surgical resection with lobectomy and nodal sampling/resection. There is randomized evidence that wedge resection is an inferior operation to lobectomy [1] but no large series randomized evidence of surgery versus any other curative intervention for early stage lung cancer. In addition, for patients over 71 years there may be no benefit of lobectomy over limited resection[2]. Stereotactic body radiotherapy (SBRT) is not a new treatment and has been used in medically inoperable stage I NSCLC for 20 years[3]. Given the very high rates of local control ~90% at 3-5 years[4], the low rates of acute toxicity and little detriment to quality of life post treatment[5] SBRT is now a standard of care for medically inoperable peripherally located T1 and T2 tumours up to 5cm in diameter. For medically operable patients where the risks of surgery are low, surgery does offer a theoretical advantage over local ablative treatment such as SBRT. Optimum surgery with removal or the tumour and surrounding lobe may remove occult cancer cells outside the treated volume that may not be included in the SBRT treatment volume. In addition, nodal resection may convey an additional survival benefit and for those patients with occult N1/2 disease those patients could further benefit with the addition of adjuvant chemotherapy.
However, the average age at the time of diagnosis of lung cancer is 70, often in patient's with significant medical co-morbidity that precludes lobectomy and reduces the chance of them receiving adjuvant chemotherapy[6]. Surgical mortality at both 30 and 90 days increases with age further reducing the potential benefit from lobectomy and nodal sampling/resection[7]. In addition, with PET/CT staging and minimally invasive techniques (EBUS) for pathologically sampling the mediastinum now routine practice, the chance of missing occult N1/N2 nodal disease is small being <9% in one series[8].
Propensity analysis of patients receiving surgery versus SBRT have been performed on retrospective series with some reports suggesting no difference in survival between the two match groups and others suggesting a benefit with surgery. Randomized controlled trials (RCT) of surgery versus SBRT (STARS/ROSEL) have been attempted but have been closed prematurely due to poor accrual. A recent pooled analysis of the STARS and ROSEL studies showed no significant difference between SBRT and surgery, though a trend for improved survival with SABR but this was based on 58 patients[9].
Given the limited data from STARS/ROSEL and conflicting results from propensity matched analysis there is a need for successful randomized trials of surgery versus SBRT to prove whether SBRT should be the standard of care. Hopefully, the open SABRtooth (UK) and STABLE-MATES (USA) trial combined with other planned trials of SBRT versus surgery will recruit and provide the answer to this key question.

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SP-0303
Against the motion
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For early-stage non-small cell lung cancer (NSCLC) surgical resection remains the treatment of choice providing excellent long-term results (1). Recently, stereotactic body radiotherapy (SBRT) has become an alternative treatment for localized NSCLC (2). SBRT has mainly been applied for functionally in operable patients with severe cardiopulmonary morbidity. Currently, there is an ongoing debate whether SBRT is also a valid oncological treatment for low-risk patients who are operable from a technical and functional perspective. No large randomized studies are available directly comparing SBRT and surgical resection with systematic lymph node dissection. Several trials closed prematurely due to poor accrual.
From a thoracic surgical point of view several concerns emerge when applying SBRT to operable early-stage NSCLC: precise pathology is not obtained in all cases, information on locoregional lymph node involvement is not always available making it difficult to recommend adjuvant chemotherapy in specific cases, and rather troublesome, different criteria are used when comparing results of surgery and SBRT, mainly in relation to local recurrence (3,4). Moreover, thoracic surgeons are more and more dealing with "salvage surgery" after previous radiotherapy when no other therapeutic options are available (5). Technically, these resections may be very challenging due to technical difficulties during dissection of the hilar region not encountered during primary intervention. These procedures should be performed in dedicated thoracic centres with a large experience.
Due to the lack of clear evidence, different opinions are expressed in present-day literature.
In a pooled analysis of two randomised trials comparing SBRT with lobectomy for stage I NSCLC that closed prematurely due to poor accrual, the authors concluded that SBRT can be considered a valid treatment option for operable stage I NSCLC (6). However, because of small patient sample size and short follow-up time, they indicate that further randomized studies should be performed before more definite recommendations can be made (6).
A different conclusion was reached in a recent propensity score analysis matching 41 patients who underwent video-assisted (VATS) lobectomy with 41 patients treated with SBRT for stage I NSCLC (7). Significant differences were found in overall survival, cause-specific survival, recurrence-free survival, local and distant control favouring VATS lobectomy. Conclusion of this study was that VATS lobectomy may offer a significantly better long-term outcome than SBRT in potentially operable patients with biopsy-proven clinical stage I NSCLC.

Another propensity score analysis compared SBRT with sublobar resection for stage I NSCLC in patients at high risk for lobectomy (8). In 53 matched pairs the difference in overall survival was not significant and the cumulative incidence of cause-specific death was comparable between both groups. Conclusion of this study was that SBRT can be an alternative treatment option to sublobar resection for patients with severe comorbidity who cannot tolerate alobectomy due to functional impairment (8).
In June 2015 the "Comité del'Evolution des Pratiques en Oncologie (CEPO) from Québec, Canada published recommendations regarding the use of SBRT (9). For medically operable patients with T1-2N0M0 NSCLC surgery remains the standard treatment due to the lack of high-level evidence and valid comparative data. For medically inoperable patients withT1-2N0M0 NSCLC or medically operable patients who refuse surgery, SBRT should be preferred to external beam radiotherapy. In the latter cases a biological equivalent dose (BED) of at least 100 Gy should be administered. The choice ofusing SBRT should be discussed within a multidisciplinary tumor board. Radiotherapy should not be considered for patients whose life expectancy is very limited because of comorbidities.
In summary, main points are:
· surgical resection remains the treatment of choice for operable early-stage NSCLC
· SBRT may be considered for functionally compromised patients who cannot tolerate lobectomy.
· further high-level evidence is needed which requires close cooperation between radiation oncologists and thoracic surgeons to design comparative trials with clear inclusion criteria and unequivocal definitions of endpoints.

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Debate: Is brachytherapy the best for partial breast irradiation?

SP-0304
Multicatheter brachytherapy is the best for APBI

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Accelerated Partial Breast Irradiation (APBI) using multicatheter brachytherapy is an attractive treatment approach not only to shorten the course of radiation therapy from 3-6 weeks to 2-5 days but also to reduce significantly the radiation exposure to the breasts, the skin, the lung and particularly to the heart very effectively.
Over the last 20 years different modalities of APBI have been introduced into clinical practice –multicatheter brachytherapy, single catheter brachytherapy, IORT techniques, different techniques of External Beam Radiation Therapy (EBRT). Unfortunately fact is that the results of APBI trials with IORT using intraoperative electrons or 50 kV photons have been negative. As well Vaidya et al. (TARGIT trial) as Veronesi et al. (ELIOT trial) reported high 5-year recurrence rate after IORT, namely 3.3%-4.4% in IORT groups versus statistically significant lower recurrence rates in control groups 0.4%-1.3%. Possibility of APBI using EBRT is of course very attractive, since this technique is broadly available and easy to perform. Unfortunately, hitherto reported results of phase 3 APBI trials using EBRT are either disappointing (RAPID trial) or with low statistical power (Olivotto et al., Livi et al.). On the contrary, during the last decade number of modern phase 2 and phase 3 APBI trials, using multicatheter interstitial brachytherapy for the delivery of APBI, have demonstrated favorable long-term local control rates and cosmetic outcomes, comparable to the results of whole breast irradiation (WBI). In the largest phase 3 randomized non-inferiority GEC-ESTRO trial with sufficient statistical power (~1200 pts.), importantly using for APBI solely multicatheter interstitial brachytherapy in 5 days, after median follow-up of 6.6 years the 5-year local recurrence rates were 1.4% in the APBI arm, and 0.9% in the WBI arm (p=0.4), and 5-year disease-free and overall survival were 96-97% in the WBI group versus 97% in the APBI group - all events are without any statistical and clinical significance. The equivalence of local recurrence rates was evident in all age groups, in all histological subgroups and also independent of the type of systemic therapy. Thus it´s the first phase 3 study proving non-inferiority of APBI in comparison to whole breast irradiation for selected early stage breast cancer patients. Undoubted is, that in the light of the landmark UK and Canadian trials comparing 5 versus 3 weeks of WBI the difference in total treatment time between WBI and APBI using multicatheter brachytherapy (4-5 days) has been partially diminished. However the difference between 3 weeks of WBI versus 4-5 days of APBI still remains clinically and socio-economically relevant. Moreover, due to the extreme steep fall-off of dose of Iridum-192, the significant dose reduction of irradiated normal tissues (including the heart and skin) is a unique advantage of interstitial multicatheter brachytherapy, which is hardly ever achievable by other APBI techniques. The remaining, hitherto unreported ongoing APBI trials unfortunately use for APBI only different techniques of EBRT. The results of these trials will therefore particularly contribute to further fine-tuning of selection criteria and to precise requirements for quality assurance of EBRT-based APBI.
In summary: At the present time only the long-term results of APBI using sole multicatheter brachytherapy for appropriate selected patients demonstrate impressive low local recurrence rates – similar as WBI, accompanying with excellent radiation protection of surrounding organs – better as WBI. Consequently "APBI used multicatheter brachytherapy is today a proven and valid alternative treatment option after breast conserving surgery, and can be offered for all low risk breast cancer patients in clinical routine".

SP-0305
IORT is the best for PBI

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Over the past ten years the results of several clinical trials have been published, detailing various approaches of PBI. Among the different techniques used, IORT has increased rapidly in popularity, mainly in Europe, and up to date many thousands of women have been treated in clinical setting. IORT allows to realize a radiation dose to the index quadrant, eliminating the treatment to the tissue remote from the tumour bed, and using only one very high dose (20 Gy or more) in a single session. When single doses above certain thresholds of 10 Gy are given, some additional biological effects on tumor cell killing and from the surrounding microenvironment can be expected. IORT also represents the possibility of overcoming some constraints such as the accessibility to the centres of radiotherapy, the socio-economic impact on the working life and on the personal habits of the patient. Another important advantage is the avoidance of the interactions with the systemic therapy, that may determine delays in the initiation or in the carrying out of the adjuvant treatment. These potential benefits must be balanced with the potential higher risk of recurrence within the untreated gland tissue in the same breast as well as the still unknown long-term results on survival and cosmesis. Two prospective randomized clinical studies establishing the role of IORT in clinical practice have been published up to now. A single-center study, named ELIOT, was performed at the European Institute for Oncology (EIO) in Milan, Italy. Patients with limited size tumor (2.5 cm) and age of 48 years or more were either randomized to a single dose of 21 Gy of IORT with electrons or to standard WBI. The local recurrence rate (LRR) at 5-years was higher in the experimental arm (4.4%